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ORIGINAL RESEARCH

Impella Versus VA-ECMO for Patients with Cardiogenic Shock: Preliminary Cost-Effectiveness Analysis in the Italian Context

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ABSTRACT

***Introduction*:** Cardiogenic shock (CS) is a life-threatening failure of the heart to supply adequate blood, requiring immediate treatment. Although nowadays Impella® heart pumps and veno-arterial extra-corporeal membrane oxygenation (VA-ECMO) are both widely employed in routine clinical practice for the management of patients with CS, extensive comparative information on their cost-effectiveness is lacking. The aim of the present study was to conduct a cost-effectiveness analysis comparing Impella to VA-ECMO in patients with CS from the National Healthcare Service (NHS) perspective in Italy. A secondary objective was to compare costs from both NHS and hospital perspectives.

***Methods*:** A Markov model projected, on a lifetime horizon, life years (LYs), quality-adjusted life years (QALYs), and costs associated with Impella and VA-ECMO. Costs from the NHS perspective were estimated mainly through Italian reimbursement rates, while hospital costs were derived from a clinical center in Italy.

***Results*:** From an NHS perspective, Impella showed lower costs and better life expectancy and patients' quality of life (€50,303, 1.544 LYs, 0.905 QALYs) compared to VA-ECMO (€76,795, 1.391 LYs, 0.784 QALYs). DRG overall reimbursements for Impella (€49,998) do not completely cover the hospital costs and the cost for the technology (€57,770). Conversely, the hospital cost for the strategy VA-ECMO (€52,190) is lower than the NHS overall reimbursements (€76,790).

***Conclusions*:** Our analysis suggests that Impella may be cost-saving over VA-ECMO, while also providing better health outcomes for patients with CS; however, discrepancies in costs

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and reimbursement rates were observed, likely due to variability in patient care and hospital resource utilization. Future real-world studies are needed to confirm these findings, but decision-makers can use this data as an initial reference for health technology assessments in Italy.

Keywords: Cardiogenic shock; Impella; VA-ECMO; Medical devices; Cost-effectiveness analysis; Hospital costs; Reimbursements

Key Summary Points

Cardiogenic shock is a critical condition characterized by severe heart failure, leading to inadequate perfusion to vital organs. Mechanical circulatory support devices such as Impella® pump or veno-arterial extracorporeal membrane oxygenation (VA-ECMO) are increasingly employed to manage cardiogenic shock patients.

Our study evaluated the cost-effectiveness of the two devices from the National Healthcare Service (NHS) perspective in Italy and compared hospital costs with DRG reimbursement rates.

Impella showed lower costs and better life expectancy, and patients' quality of life compared to VA-ECMO. Reimbursement rates for Impella in Italy do not completely cover the hospital costs and the cost for the technology.

INTRODUCTION

Cardiogenic shock (CS) is a severe medical condition that occurs when the heart is unable to pump adequate blood to meet the body's requirements, leading to inadequate perfusion of organs and tissues. It is a life-threatening condition that requires prompt medical care [1]. CS is associated with a severe primary dysfunction of the heart, often resulting from acute myocardial infarction, or can be caused by other cardiac disorders such as cardiomyopathy or severe arrhythmias. The incidence of CS among patients with acute myocardial infarction is up to 10% [2].

Key features of CS include a rapid decline in blood pressure, decreased cardiac output, and compromised tissue perfusion. The severity of symptoms can escalate rapidly, necessitating immediate intervention, since severity of CS presentation correlates with outcomes [3]. The therapeutic approach to CS may include medications to improve heart function and/or mechanical support devices to assist the heart in pumping blood.

The utilization of short-term mechanical circulatory support (MCS) has become extensive in the treatment of CS and has been granted a Class IIA recommendation in the latest Heart Failure guidelines from the European Society of Cardiology [4]. The main recommended devices are the Impella® heart pump, manufactured by Abiomed, a Johnson & Johnson company, and veno-arterial extracorporeal membrane oxygenation(VA-ECMO), while intra-aortic balloon pump (IABP) is not routinely suggested in AMI-CS [4].

Impella is a weanable MCS device designed to provide temporary assistance to the heart in patients experiencing CS. It is a microaxial flow pump that is inserted via transaortic route into the heart to increase forward flow providing at the same time powerful ventricular unloading [5]. While the Impella device can be lifesaving, it is not without risks. Complications may include bleeding, vascular injury, and device-related issues [6]. Observational studies have suggested valuable survival rates with Impella use in cardiogenic shock [7–9] and a recent large-scale clinical trial has suggested survival benefit in specific populations [10].

VA-ECMO is an advanced life support system that provides both cardiac and respiratory assistance to patients with CS whose heart and lungs are severely compromised. With this device for biventricular support, the blood is withdrawn from a central vein, oxygenated and then returned to a central artery.

The choice of the device for MCS is based on clinical information such as the patient's overall condition, the cause and phenotype of CS, and

the potential benefits and risks of mechanical support. Although nowadays Impella and VA-ECMO are both widely employed in routine clinical practice, extensive comparative information on their cost-effectiveness is lacking in the area of CS.

The overall aim of the present study was to measure the added value of Impella, and to compare it to VA-ECMO, to inform decision-makers on the choices offered for managing patients with CS. In particular, the aim of the present study was to perform a cost-effectiveness analysis (CEA) comparing the two medical devices from the National Healthcare Service (NHS) perspective in Italy. Furthermore, hospital costs for both strategies were compared with the DRG reimbursement rates. No recent studies comparing the cost-effectiveness of Impella against VA-ECMO for the treatment of patients with CS are available in any country, highlighting the gap of evidence to inform reimbursement decisions spans several geographical settings. Conducting this analysis in the Italian setting represents the occasion to start collecting evidence in this area, in view of the recent EU HTA Regulation [11, 12] and the Italian Program of HTA for Medical Devices [13] by leveraging the fact that the country hosts several highly specialized and high-volume centers that use both devices.

METHODS

The Model

A Markov model has been selected for this economic evaluation and developed to project quality-adjusted life years (QALYs) and costs associated with Impella and VA-ECMO for managing patients with CS (as defined by INTERMACS Class 1-2-3 or SCAI Class C-D-E [14]). The analysis has been reported according to the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) (see Supplementary Material) [15]. Ethics approval and informed consent were not needed for this study because the data used for the analyses were derived exclusively from studies published in the literature.

The health states considered in the implemented model were: (i) "CS", (ii) "Adverse events", and (iii) "Death for disease" (Fig. 1). Adverse events that include stroke, bleeding, limb ischemia, and renal failure, all directly

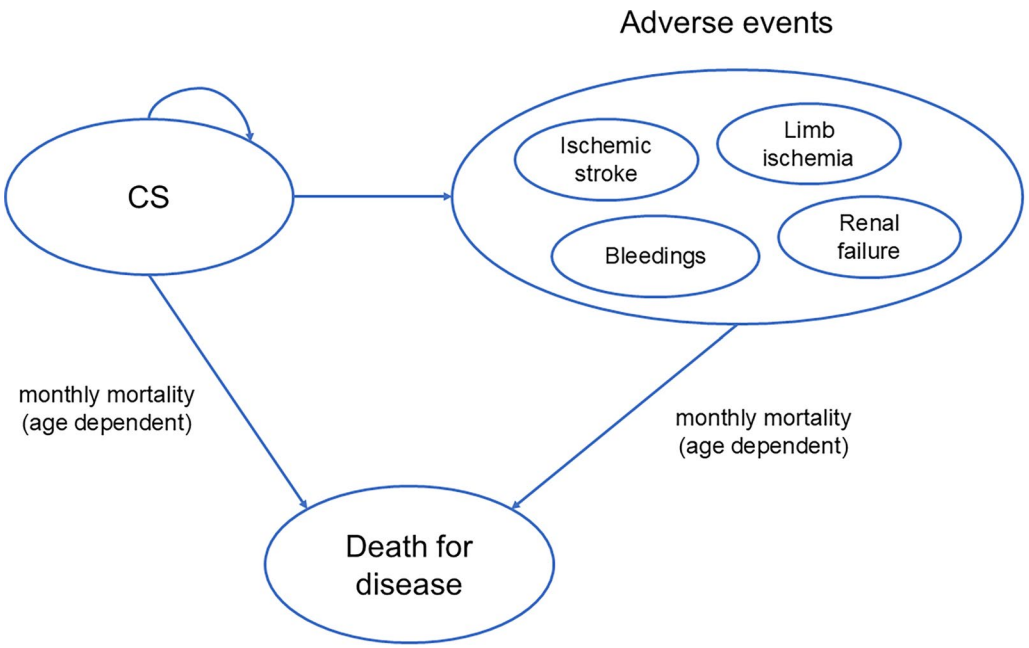

Fig. 1 Representation of the model (*CS* cardiogenic shock)

linked with healthcare resource consumption (and consequently costs), have been considered as part of the current economic evaluation. To ensure outcome comparability, only access-site bleeding and major bleeding (or equivalent) were considered. A major bleeding refers to a significant loss of blood, generally requiring transfusion, that can result in serious complications, including shock or death, if not treated promptly.

The model considers a hypothetical cohort of patients with CS with a mean age of 59 years, as reported in the literature [16] (see next paragraph "Comparative clinical data"). They start the Markov process in the "CS" state. Patients may stay in this state or, in case of adverse events, may move to the "Adverse events" state. It has been assumed that adverse events happen in the first 30 days of treatment with Impella or VA-ECMO, considering that most of the studies used in a meta-analysis by Ardito et al. [16] referred to the hospitalization period. An exponential function has been applied for overall survival data emerging from the same meta-analysis [16]. The model also takes into account background mortality according to Italian life tables [17]. The model calculations ensure that the overall mortality is always higher than, or equal to, the background mortality for the Italian population. A cycle length of 30 days and a lifetime horizon have been chosen for the baseline analysis. A discount rate of 3% has been applied to costs and health outcomes [18]. The model has been implemented using Microsoft Excel.

Data Sources

Comparative Clinical Data

This study is a literature-based CEA. A recently published systematic literature review with meta-analyses has been used as the source of data for the comparison of Impella versus VA-ECMO used as a standalone device (not in combination) in the treatment of CS [16]. This study considered randomized controlled trials (RCTs), prospective clinical trials and observational studies. The study selection criteria for the meta-analyses were designed to maximize the homogeneity of device usage characteristics, specifically including studies where a single device was used for managing adult patients with cardiogenic shock between 2017 and 2022. This approach aimed to minimize biases related to potential technological advancements over time. The population considered in the systematic literature review had an average age of 59 years and was mainly composed of male patients (70.8%). Mortality at 1 year was reported as 48% and 52% for Impella and VA-ECMO, respectively. Major and access site bleedings during the hospitalization totaled 19% for Impella and 23% for VA-ECMO, while limb ischemia was present in 6% of patients treated with Impella and 10% of patients treated with VA-ECMO. Finally, ischemic stroke during hospitalization was more likely to occur in patients treated with VA-ECMO (6%) than in those treated with Impella (2%). Likewise, renal failure events were slightly more frequent in the populations treated with VA-ECMO (38%) compared to Impella (34%).

Regarding the possibility of device malfunction, the DanGer Shock trial [10], which compared Impella to medical treatment in patients with cardiogenic shock CS, reported a device malfunction rate of 1.2%. This rate was incorporated into the model, including the associated re-implantation cost. To maintain a conservative approach, failure rates for VA-ECMO were not included. Table 1 summarizes the model inputs.

Healthcare Resource Consumption and Costs

Direct healthcare resource consumption (direct costs) was accounted for in the model (Euros, 2024). To reflect the Italian NHS perspective, cost data were derived from national diagnosis-related group (DRG) reimbursement rates for the utilization of the devices (Table 2). Since the frequencies of complications considered in the model pertain to the hospitalization period for managing CS, no additional DRG reimbursements needed to be applied, since the cost for their management is included in either Impella or VA-ECMO DRGs.

From the hospital perspective, costs were based on the cost function linked to the different production factors. Since the IRCCS (Istituto di

Table 1 Summary of model inputs with information on the distributions used in the probabilistic sensitivity analysis

Parameter	Value	Standard error of the mean	Distribution type	Alpha/ mean of logs	Beta/lambda/ standard error of logs	References
Discount rate	3%	0.01	Beta	24.22	783.11	PE Guidelines Around The World: Italy [18]
Age (years)	59	11.800	Gamma	25.000	2.360	Ardito 2023 [16]
Males (%)	0.71	0.142	Beta	6.592	2.719	Ardito 2023 [16]
Utility values						
Utility value Impella	0.67	0.055	Beta	48.301	23.790	Roos 2013 [19]
Utility value VA-ECMO	0.67	0.055	Beta	48.301	23.790	Roos 2013 [19]
Utility value renal failure (hemodialysis)	0.44	0.088	Beta	13.503	17.033	Roos 2013 [19], Haller 2011 [20]
Utility value ischemic stroke	0.31	0.046	Beta	31.027	69.060	Roos 2013 [19]
Disutility major bleedings	0.37	0.030	Beta	95.460	162.540	Roos 2013 [19]
Disutility limb ischemia	0.06	0.012	Beta	23.466	374.263	Pietzsch 2022 [21]
Adverse events (% of patients)						
Impella major bleedings	0.19	0.033	Gamma	32.824	0.006	Ardito 2023 [16]
Impella limb ischemia	0.06	0.012	Gamma	25.000	0.002	Ardito 2023 [16]
Impella ischemic stroke (hospital)	0.02	0.005	Gamma	15.366	0.001	Ardito 2023 [16]
Impella renal failure (hospital)	0.32	0.046	Gamma	48.565	0.007	Ardito 2023 [16]
VA-ECMO major bleedings	0.23	0.028	Gamma	67.180	0.003	Ardito 2023 [16]
VA-ECMO limb ischemia	0.10	0.020	Gamma	25.000	0.004	Ardito 2023 [16]
VA-ECMO ischemic stroke (hospital)	0.06	0.013	Gamma	22.128	0.003	Ardito 2023 [16]
VA-ECMO renal failure (hospital)	0.35	0.028	Gamma	155.569	0.002	Ardito 2023 [16]

Table 1 continued

Parameter	Value	Standard error of the mean	Distribution type	Alpha/ mean of logs	Beta/lambda/ standard error of logs	References
Timing						
Duration bleedings (days)	30.00	6.000	Gamma	25.000	1.200	Assumption
Duration limb ischemia (days)	30.00	6.000	Gamma	25.000	1.200	Assumption
Days on Impella*	3.23	0.646	Gamma	25.000	0.129	Ardito 2023 [16]
Days on VA-ECMO*	4.47	0.894	Gamma	25.000	0.179	Ardito 2023 [16]
Major bleedings: *N* days ICU*	3	0.600	Gamma	25.000	0.120	San Raffaele Scientific Institute
Limb ischemia: *N* days ICU*	2	0.400	Gamma	25.000	0.080	San Raffaele Scientific Institute
Ischemic stroke: *N* days ICU*	5	1.000	Gamma	25.000	0.200	San Raffaele Scientific Institute
NHS perspective costs						
Cost Impella (DRG 104)	24,675	4935.000	Gamma	25.000	987.000	DRG national tariff
Cost VA-ECMO (DRG 541)	51,919	10,383.800	Gamma	25.000	2076.760	DRG national tariff
Ischemic stroke: FUP monthly cost (1–3 months)	1420	283.968	Gamma	25.000	56.794	Fattore 2012 [22]
Ischemic stroke: FUP monthly cost (4–6 months)	358	71.604	Gamma	25.000	14.321	Fattore 2012 [22]
Ischemic stroke: FUP monthly cost (7–12 months)	186	37.226	Gamma	25.000	7.445	Fattore 2012 [22]
Renal failure: FUP monthly cost	4610	921.990	Gamma	25.000	184.398	Ingrasciotta 2021 [23]

CT computed tomography, *ICU* intensive care unit, *FUP* follow-up

*Data used to estimate hospital costs

Ricovero e Cura a Carattere Scientifico—Italian acronym for research hospitals) San Raffaele Scientific Institute in Milan is a tertiary care center for CS in Italy, the hospital costs of this clinical center have been considered a proxy for hospital costs in the Italian setting. In particular, for the management of the different adverse events, a list of activities and healthcare resources based

Table 2 DRG reimbursement rates considered in the model (NHS perspective)

Item	Cost (€)	Reference
Impella	24,675	DRG 104
VA-ECMO	51,919	DRG 541

DRG diagnosis-related group

on the clinical practice were identified by the clinicians of the center (MP, MS) (Table 3), based on clinical record charts review. Therefore, costs derived from the administrative office of San Raffaele Scientific Institute were applied.

To consider long-term costs for the management of patients with stroke or renal failure in Italy, we referred to the published literature. In particular, costs of 1420€, 358€ and 185€ (uplifted to year 2024) were retrieved for the monthly post-discharge follow-up of patients with stroke in the periods 1–3 months, 4–6 months and 7–12 months, respectively [22]. Regarding renal failure, from the Italian study by Ingrasciotta and colleagues [23], the monthly management cost of 4610€ (uplifted to 2024)

Table 3 Cost items considered for the management of adverse events during the hospitalization (used only for the hospital costing calculations)

Adverse event	Item	Cost (€)
Limb ischemia	Drugs	27.50
	Disposables	238.21
	Imaging (ultrasound)	105.58
	Healthcare personnel	467.70
	Direct costs	219.91
	Indirect costs	177.16
	2 days in ICU	3757.62
Ischemic stroke	Imaging (3 CT brain scan)	479.79
	1-day mechanical ventilation	24.86
	Healthcare personnel (5 neurological consultancies and psychological support for 3 months)	340.50
	5 days in ICU	9394.05
	3 months physiotherapy	1206.40
Major/access site bleeding	Interventional procedure	651.19
	Imaging (1 ultrasound, 1 CT scan)	244.03
	Transfusions	846.92
	3 days in ICU	5636.43
Renal failure	Dialysis/disposables	371.86
	Healthcare personnel (1 nephrologist and 1 nurse)	48.15
	Direct costs	28.85
	6 days in ICU	11,272.85

CT computed tomography, *ICU* intensive care unit

has been retrieved. These follow-up costs have been considered for both NHS and hospital perspectives due to the lack of more specific data. For the NHS perspective, only direct costs borne by the NHS were included (and not societal or informal costs).

Regarding the devices, the model accommodated the use of either Impella CP® heart pump or Impella 5.5® heart pump, with associated list prices for the Italian market provided by the manufacturer (Impella CP: €17,500 + 4% VAT; Impella 5.5: €37,000 + 4% VAT). The usage percentage of the Impella CP (90%) was based on 5-year extrapolations from data reported in the study by Chieffo and colleagues [24], which reported statistics on the multicenter observational Italian registry IMP-IT for the management of patients with CS; considering that versions Impella 2.5® heart pump and Impella 5.0® heart pump are currently out of market, the remaining market share was assigned to the Impella 5.5 (10%). Since the implantation of the Impella 5.5 is performed in the operating room, an additional cost of 1431.76€ was considered for this type of device.

The hospital cost for VA-ECMO has been estimated as the mean cost per patient reported in a few public tenders in Italian Regions. This cost is composed by a component for consumables (9463€ per patient) and a fixed amount for the device (2466€ per patient), for a total cost per patient of 11,930€. These costs are summarized in Table 4.

Quality of Life Estimates

Studies reporting data on patients' quality of life have been searched in the literature as well, and three relevant sources were retrieved. The study by Roos et al. [19] reported a utility coefficient of 0.67 for the CS state and utilities of 0.31 for stroke and 0.30 for major bleeding. Another study reported a disutility for limb ischemia of 0.059 [21]. For renal failure a utility value of 0.66 was applied [20] to the CS state, leading to a value of 0.44. Disutilities were applied for the duration of events, estimated in 30 days according to the duration of hospitalization. All the model inputs are summarized in Table 1.

Cost-Effectiveness Analyses

Costs and QALYs for the strategies considered were estimated to calculate the incremental cost-effectiveness ratio (ICER) and incremental cost-utility ratio (ICUR) of Impella versus VA-ECMO. In Italy, willingness-to-pay (WTP) thresholds vary between 25,000€ and 60,000€ [25, 26], therefore in the context of the present analysis an intermediate WTP of 50,000€/QALY has been applied.

Table 4 Assessment of the cost for VA-ECMO per patient

Tender	Rental VA-ECMO device (12 months) (€)	Purchasing cost VA-ECMO (€)	Number of foreseen patients	Device cost per patient (€)	Consumables* cost per patient (€)
Emilia-Romagna Region (Parma)	33,996		20	1700	8200
Friuli-Venezia Giulia Region		178,750	200	894	7000
Campania Region (a)					10,500
Campania Region (b)	36,960		100	370	8198
Liguria Region	48,312		7	6902	13,419
Mean value				2466	9463

*Circuit, venous and arterial tubes, insertion kit

Model parameters were incorporated along with specific probability distributions: a beta distribution for utilities and the proportions of patients experiencing adverse events, and a gamma distribution for costs. Variations in model parameters were based on 95% confidence intervals, standard deviations, or ranges reported in meta-analyses [16] and other reference studies. For parameters without reported variation information, a ± 50% variation from the baseline value was applied.

To assess the robustness of the model results, both deterministic sensitivity analysis (DSA) and probabilistic sensitivity analysis (PSA) were conducted. In PSA, second-order Monte Carlo simulations (10,000 iterations) were performed to account for parameter variability. Additionally, one-way sensitivity analyses were carried out using the same parameter variations as in PSA, except for the discount rate, which was varied from 0 to 10%.

RESULTS

Cost-Effectiveness Analysis Results

Considering a lifetime horizon and the NHS perspective, for Impella the average QALYs were estimated to be 0.905 (LYs 1.544); for VA-ECMO, the average QALYs were 0.784 (LYs 1.391). The mean cost per patient for Impella was estimated to be 50,303€, while for VA-ECMO a cost of 76,795€ was obtained. Impella was the dominant strategy (i.e., less costly and with higher LYs and QALYs) compared to VA-ECMO showing a negative ICER (– 173,186€/LY) and ICUR (– 218,607€/QALY). The model results are summarized in Table 5.

From the hospital perspective, the mean costs for a patient treated with Impella and VA-ECMO were 57,770€ and 52,190€, respectively. From the NHS perspective, the probabilistic sensitivity analysis (Fig. 2) indicates that Impella may be a cost-effective option compared to VA-ECMO, as it remains cost-effective in nearly all simulations within a WTP threshold range of 0 to 100,000€/QALY.

One-way variations on the model parameters are represented by a tornado diagram (Fig. 3). Parameter variations did not alter the dominance of Impella over VA-ECMO (as shown by the negative ranges of the ICUR in the diagram), except for variations in mortality rates for both devices, which resulted in a positive ICUR. Specifically, when the 1-year mortality rate for Impella is set at 67% (the upper bound of the 95% CI), the model estimates 0.561 QALYs (0.961 LYs) at a cost of 39,993€. In this scenario, VA-ECMO incurs higher costs and yields a greater number of QALYs compared to Impella. Consequently, the incremental cost-utility ratio (ICUR) for VA-ECMO versus Impella is 165,243€, which exceeds the cost-effectiveness threshold of 50,000€/QALY, thereby confirming the cost-effectiveness of Impella. Similarly, when the 1-year mortality rate for VA-ECMO is set at 36% (the lower bound of the 95% CI), the model estimates for this strategy 1.233 QALYs (2.181 LYs) at a cost of 92,121€ and an ICUR for VA-ECMO versus Impella of 127,566€, further supporting the cost-effectiveness of Impella.

Table 5 Cost-effectiveness results from the NHS perspective (lifetime horizon)

Expected outcomes	Impella	VA-ECMO	Difference (Impella-VA-ECMO)	ICER Impella vs. VA-ECMO	ICUR Impella vs. VA-ECMO
Costs	50,303€	76,795€	– 26,492€	– 173,186€/LY (Impella dominant)	– 218,607€/QALY (Impella dominant)
LYs	1.544	1.391	0.153		
QALYs	0.905	0.784	0.121		

ICER incremental cost-effectiveness ratio, *ICUR* incremental cost-utility ratio, *LY* life years, *QALY* quality-adjusted life years

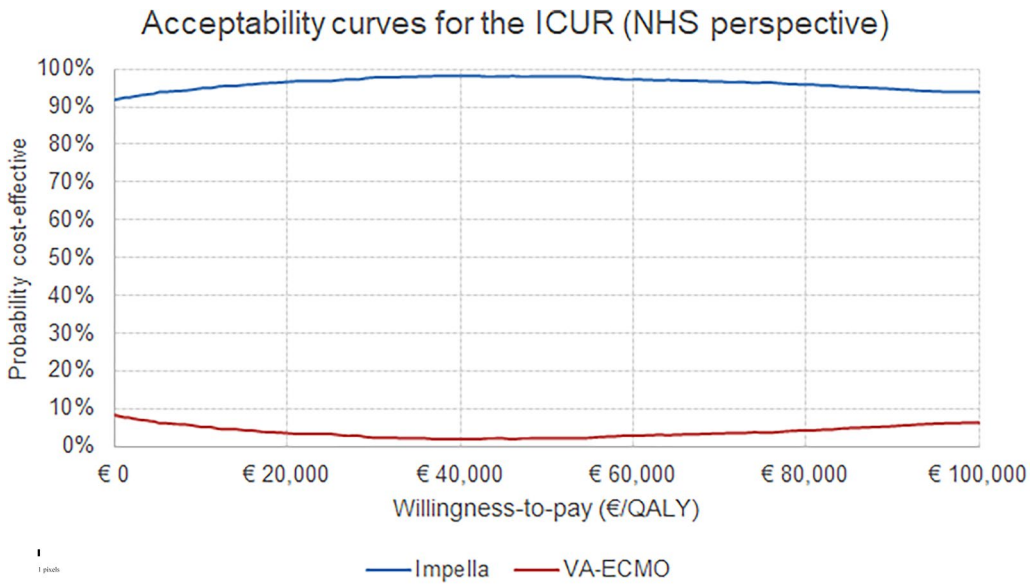

Fig. 2 Acceptability curves for the ICUR

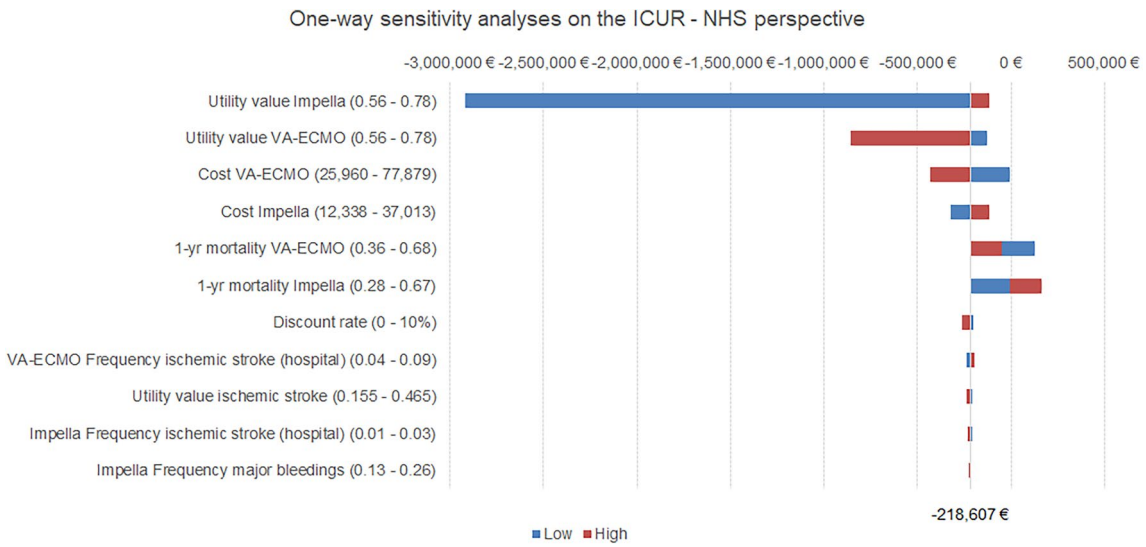

Fig. 3 Tornado diagram showing one-way sensitivity analyses on the ICUR

DISCUSSION

The present study aimed to evaluate the cost-effectiveness of Impella vs. VA-ECMO to assess the value of currently available medical devices for the management of patients with CS in the clinical practice in Italy. Impella and VA-ECMO are advanced MCS devices used for the management of patients with CS. The economic impact related to the use of these devices is quite high since they require the management of specialized equipment in operating rooms by a team of experts in acute cardiac care. So far, comprehensive economic evaluations comparing Impella to VA-ECMO are limited.

Since relying solely on reimbursement rates to quantify the costs of MCS devices and the

management of adverse events may provide a limited perspective on the actual expenses incurred by hospitals, our analysis compared costs from both the NHS and hospital perspectives to generate more accurate estimates.

The results suggest that Impella could be a cost-saving strategy in comparison to VA-ECMO from an Italian Healthcare Service perspective. Furthermore, the probabilistic sensitivity analysis confirmed the robustness of the results, with nearly the totality of the simulations lying below the commonly accepted ICUR threshold representing value for money. Our results are in line with the ones presented in the literature in comparable settings. A French study [27] performed a budget impact analysis comparing Impella to VA-ECMO; the authors stated that over a time horizon of 5 years, the introduction of Impella 5.0 was associated with cumulative savings of €4.3 million. The results were driven by the lower risk of device-related complications associated with Impella 5.0. According to a different study [28], Impella showed shorter hospital stays (7 days vs. 11 days) and reduced expenses ($66,078 vs. $122,996) compared to ECMO.

From an effectiveness perspective, Impella demonstrated superior survival outcomes compared to VA-ECMO, with 1.544 life years versus 1.391 life years, respectively. This difference suggests that Impella is associated with improved long-term outcomes, potentially due to reduced mortality and better cardiogenic shock management. Additionally, patients treated with Impella achieved a higher QALY score of 0.905, compared to 0.784 for VA-ECMO, indicating not only prolonged survival but also a higher quality of life. This may be attributed to lower complications rate, shorter hospital stays, and better post-treatment functional status. The superior QALY outcome further suggests that Impella supports faster recovery, enhanced physical functioning, and a lower incidence of adverse events, such as organ dysfunction, compared to VA-ECMO.

The results provided in terms of mean costs per patient for the management of CS with Impella or VA-ECMO from both NHS and hospital perspectives allow further analyses. Considering that our model compares the two devices for the management of patients with the same clinical characteristics (i.e., CS defined by INTERMACS Class 1-2-3 or SCAI Class C-D-E), the hospital perspective seems reflecting quite similar costs for the two clinical pathways (€57,770 for Impella vs. €52,190 for VA-ECMO). The cost for the strategy Impella in the hospital perspective is higher compared to the NHS perspective (57,770€ vs. 50,303€), meaning that the DRGs reimbursements does not completely cover the hospital costs and the cost for the technology. Indeed, increasing Impella reimbursement by an average of 7467€ to fully cover the cost does not change the dominant result. Deterministic dominance was maintained with a price of Impella up to 50,853€, while a price lower than 56,841€ kept the Impella strategy below the 50,000€/QALY threshold. Conversely, the cost for the strategy VA-ECMO is lower in the hospital perspective compared to the NHS one. This may be due to reimbursement rates that are estimated considering more complex clinical cases. Another reason may be related to the wide variation of costs among hospitals due to differences in efficiency, personnel costs, supply prices, and other operational factors. DRG rates aim to average out these differences, potentially leading to overpayment for more efficient hospitals. The formulation of reimbursement policies for technological innovations normally follows the HTA process (as also stated by the Italian PNHTADM [13]). Therefore, it is not unexpected that the current DRG reimbursement for Impella is not sufficient, as a cost-effectiveness analysis of the new technology had never been carried out. Thus, studies like this are relevant to suggest modifications to the reimbursement policies to policymakers, while remaining aware that reimbursement policies are not solely aimed at covering production costs but also at influencing the behavior of providers and prescribers.

The present study has a few limitations that need to be documented. First of all, the clinical effectiveness and the rates of adverse events were derived from published meta-analyses [16] based on randomized controlled trials (RCTs), prospective clinical trials, and observational studies. Although the latter have some limitations compared with RCTs, such studies can anyway offer valuable real-world evidence (RWE) on the use of the technology [29, 30]. If from one side meta-analyses can provide valuable insights

by combining and analyzing data from multiple studies, there may be challenges associated with the variability in the study populations or methodologies applied to obtain outcomes. Another point relates to the fact that studies with positive results are more likely to be published, leading to possible publication bias as an overestimation of effects when negative or null results are not included.

Complications arising from device implantation may necessitate additional interventions that, especially in the long term, can increase the overall costs. The analysis considered the management of the main complications but an extensive evaluation of a wider range of possible adverse events could have provided a comprehensive picture of the cost-effectiveness of Impella. For example, the model did not consider the possibility of amputation as a consequence of limb ischemia. While this event could increase healthcare costs, the literature [31] reports it as an extremely rare occurrence in a population without specific risk factors but experiencing cardiogenic shock, with a risk of 0.2%. This is because other therapies, if administered promptly, can help preserve the limb. Another argument regards the estimation of healthcare resource use for the cost analysis from the hospital perspective. In the current study, we relied on standard pathways for the management of the main complications in the clinical center analyzed (IRCCS San Raffaele), which is considered one of the excellence centers in Italy for the management of patients on MCS. For this reason, hospital costs may be lower compared to other hospitals due to greater efficiency, therefore the generalizability of the data to other settings should be made with caution. Regarding the management of patients with limb ischemia, the model did not include the cost of wound care during follow-up. However, since the percentage of patients with this complication is higher for VA-ECMO compared to Impella, the model results should be considered conservative. Clinical outcomes and resource consumption related to patients managed with new technologies, such as ventricular assist devices, may be influenced by the underlying learning curve related to the experience of the operators [32]. Continuous monitoring and data collection could provide more robust evidence for the evaluation of this aspect.

The analysis considered direct healthcare costs and excluded patients' productivity losses in the post-implant period and out-of-pocket costs related to formal or informal care, which may be significant for the category of patients under investigation. We have planned to gather these specific data directly from patients according to a published protocol [33] that will be able to offer a more comprehensive understanding of the cost-effectiveness profile of Impella.

In the post-CS period, we considered patients' quality of life depending only on the likelihood of experiencing adverse events, as the literature lacks specific quality-of-life data for the implanted devices. In this context, generating accurate evidence directly from patients through the cited protocol [33] would be crucial to measure quality-adjusted life years for comparative purposes.

Lastly, in clinical practice, the choice of the device for CS treatment is strongly dependent on patients' characteristics and the clinical condition at time of presentation in order to maximize the benefits of such therapy. The present study is not intended to override clinical decision-making, rather to provide important information to raise awareness of the cost-effectiveness of available therapies that may influence the medical approach. Furthermore, it should be noted that, in clinical practice, a combination of MCS devices, such as the combined configuration of VA-ECMO and Impella (ECPella), is often used to manage patients with CS. However, in our analysis, to avoid confounding factors, we directly compared Impella to VA-ECMO. In the future, a broader analysis based on real-world data (RWD) will provide more accurate results on the different pathways, including those involving multiple devices, to identify the best cost-effectiveness profile for the management of patients with CS.

CONCLUSIONS

The cost-effectiveness of Impella versus VA-ECMO is a nuanced consideration that involves

a balance between clinical effectiveness, resource utilization, and economic factors. The choice between these devices is made based on the specific clinical context and the goals of therapy for individual patients.

The present study showed that Impella may be considered a cost-saving option compared to VA-ECMO for the management of patients with CS from the NHS perspective. The assessment of medical devices presents distinct challenges compared to drugs, including the complexity of evaluation, the impact of operators' learning curves, the heterogeneity of devices, the need for robust post-market surveillance, and navigating regulatory pathways [34]. In this context, the production of RWE can sometimes be more meaningful for policy makers in comparison to randomized controlled trials [32]. In the future, real-world studies comparing Impella to VA-ECMO will enhance the clinical evidence necessary to confirm or contest the validity of this preliminary evaluation. In the meantime, decision-makers may look at these preliminary results as a first reference for HTA considerations in this specific patients' population [12].

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Declarations

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